

WHAT IS CLAIMED IS:

1. A purified and isolated polynucleotide sequence consisting essentially of polynucleotide sequence encoding a mammalian Ca^{2+} /calmodulin stimulated cyclic nucleotide phosphodiesterase polypeptide.
2. A purified and isolated polynucleotide sequence consisting essentially of polynucleotide sequence encoding a mammalian cyclic GMP stimulated cyclic nucleotide phosphodiesterase polypeptide.
3. A polynucleotide sequence according to claim 1 or 2 which encodes a human phosphodiesterase polypeptide.
4. A polynucleotide sequence according to claim 3 selected from the group consisting of the human DNA inserts present in vectors pGSPDE6.1 (A.T.C.C. 68583), pGSPDE7.1 (A.T.C.C. 68585), pGSPDE9.2 (A.T.C.C. 68584), λ CaM H6a (A.T.C.C. 75000) pcamH3EF (A.T.C.C. 68964), pHcam61-6N-7 (A.T.C.C. 68963), pcamHella (A.T.C.C. 68965), and pHcgs6n (A.T.C.C. 68962).
5. A polynucleotide sequence according to claim 1 or 2 which encodes a bovine phosphodiesterase polypeptide.
6. A polynucleotide sequence according to claim 5 which encodes a bovine brain 61 kDa Ca^{2+} /calmodulin stimulated phosphodiesterase polypeptide.
7. A polynucleotide sequence according to claim 5 encoding a bovine brain 63 kDa Ca^{2+} /calmodulin stimulated phosphodiesterase polypeptide.

8. A polynucleotide sequence according to claim 5 which encodes a bovine heart 59 kDa Ca^{2+} /calmodulin stimulated phosphodiesterase polypeptide.

5 9. A DNA sequence according to claim 8 which is SEQ ID NO: 16.

10 10. A DNA sequence according to claim 5 selected from the group consisting of the bovine DNA inserts present in vectors p12.3A (A.T.C.C. 68577), pCaM-40 (A.T.C.C. 68576), pBBCGS PDE-5 (A.T.C.C. 68578), pBBCGS PDE-7 (A.T.C.C. 68580), and p3CGS-5 (A.T.C.C. 68579).

11. A cDNA sequence according to claims 1 or 2.

15 12. A genomic DNA sequence according to claims 1 or 2.

13. A DNA vector having inserted therein a DNA sequence according to claim 1 or 2.

20 14. A procaryotic or eucaryotic host cell stably transformed with a polynucleotide sequence according to claim 1 or 2.

15. A yeast host cell according to claim 14.

16. A polypeptide product of the expression in a transformed procaryotic or eucaryotic host cell of a polynucleotide sequence according to claim 1 or 2.

25 17. A polypeptide product according to claim 16 as expressed in a yeast host cell.

18. A purified and isolated polynucleotide sequence consisting essentially of a polynucleotide sequence encoding a polypeptide having the enzymatic activity of a mammalian Ca^{2+} /calmodulin stimulated cyclic nucleotide phosphodiesterase and selected from the group consisting of:

(a) the mammalian DNA inserts in vectors pCAM-40 (A.T.C.C. 68576), p12.3 (A.T.C.C. 68577), and pHcam61-6N-7 (A.T.C.C. 68963);

(b) polynucleotide sequences which hybridize under stringent hybridization conditions to a DNA sequence selected from the mammalian DNA inserts in vectors pCAM-40 (A.T.C.C. 68576), p12.3A (A.T.C.C. 68577), λ CAM H6a (A.T.C.C. 75000), pHcam61-6N-7 (A.T.C.C. 68963), pcamH3EF (A.T.C.C. 68964), and pcamHella (A.T.C.C. 68965);

(c) polynucleotide sequences which hybridize under stringent hybridization conditions to the sequence set forth in SEQ ID NO: 16;

(d) polynucleotide sequences encoding the same polypeptide as the polynucleotide sequences of (a), (b) and (c) above by means of degenerate codons.

19. A polypeptide product of the expression in a transformed or transfected procaryotic or eucaryotic host cell of a polynucleotide sequence according to claim 18.

20. A polypeptide product according to claim 19 as expressed in a yeast host cell.

21. A purified and isolated polynucleotide sequence consisting essentially of a polynucleotide sequence encoding a polypeptide having the enzymatic activity of a mammalian cyclic GMP stimulated nucleotide

phosphodiesterase and selected from the group consisting of:

- (a) the mammalian DNA inserts in vectors p3CGS-5 (A.T.C.C. 68579) and pHcgs6n (A.T.C.C. 68962);
- 5 (b) polynucleotide sequences which hybridize under stringent hybridization conditions to the mammalian DNA inserts in vectors p3CGS-5 (A.T.C.C. 68579), pHcgs6n (A.T.C.C. 68962), pGSPDE6.1 (A.T.C.C. 68583), pGSPDE7.1 (A.T.C.C. 68585), pGSPDE9.2 (A.T.C.C. 68584), pBBCGSPDE-5
10 (A.T.C.C. 68578) and pBBCGSPDE-7 (A.T.C.C. 68580); and
- (c) DNA sequences encoding the same polypeptide as the DNA sequences of (a) and (b) above by means of degenerate codons.

22. A polypeptide product of the expression in
15 a transformed or transfected procaryotic or eucaryotic host cell of a polynucleotide sequence according to claim 21.

23. A polypeptide product according to claim 22 as expressed in a yeast host cell.

20 24. An antibody substance specifically immunoreactive with a polypeptide product according to claim 16, 19 or 22.

25 - 25. A method for producing a polypeptide having the enzymatic activity of a mammalian Ca^{2+} /calmodulin stimulated cyclic nucleotide phosphodiesterase, said method comprising:

- (a) stably transforming or transfecting a procaryotic or eucaryotic host cell with a polynucleotide sequence according to claim 1 or 18; and

(b) growing the host cell formed in step (a) in a nutrient medium under conditions allowing expression of said DNA sequence in said host cell.

5 26. A method according to claim 25 further including the step of isolating the polypeptide product of expression of said polynucleotide sequence in said host cell.

 27. A method according to claim 25 wherein said host cell is a yeast host cell.

10 28. A method for producing a polypeptide having the enzymatic activity of a cyclic GMP stimulated cyclic nucleotide phosphodiesterase, said method comprising:

15 (a) stably transforming or transfecting a procaryotic or eucaryotic host cell with a polynucleotide sequence according to claim 2 or 21; and

 (b) growing the host cell formed in step (a) in a nutrient medium under conditions allowing expression of said DNA sequence in said host cell.

20 29. A method according to claim 28 further including the step of isolating the polypeptide product of expression of said polynucleotide sequence in said host cell.

25 30. A method according to claim 28 wherein said host cell is a yeast host cell.

 31. An assay method for identifying a chemical agent which modifies the enzymatic activity of a mammalian Ca^{2+} /calmodulin sensitive cyclic nucleotide phosphodiesterase, said method comprising:

5 (a) stably transforming, with a polynucleotide sequence according to claim 1 or 18, a procaryotic or eucaryotic host cell having a phenotypic character susceptible to alteration upon expression of said polynucleotide sequence;

10 (b) growing the host cell formed in step (a) in a nutrient medium under conditions allowing expression of said polynucleotide sequence in said host cell accompanied by the corresponding alteration in the host cell phenotype;

(c) contacting the host cells grown according to step (b) with a chemical agent to be assayed; and,

15 (d) determining any modification in the alteration of the phenotype of said host cells contacted with said chemical agent in step (c).

32. An assay method according to claim 31 wherein said host cell is a yeast host cell.

20 33. An assay method for identifying a chemical agent which modifies the enzymatic activity of a mammalian cyclic GMP stimulated cyclic nucleotide phosphodiesterase, said method comprising:

25 (a) stably transforming, with a polynucleotide sequence according to claim 2 or 21, a procaryotic or eucaryotic host cell having a phenotypic character susceptible to alteration upon expression of said polynucleotide sequence in said host;

30 (b) growing the host cell formed in step (a) in a nutrient medium under conditions allowing expression of said polynucleotide sequence in said host cell accompanied by the corresponding alteration in the host cell phenotype;

(c) contacting the host cells grown according to step (b) with a chemical agent to be assayed; and,

(d) determining any modification in the alteration of the phenotype of said host cells contacted with said chemical agent in step (d).

5 34. An assay method according to claim 33 wherein the host cell is a yeast host cell.

35. An assay method for identifying a chemical agent which modifies the enzymatic activity of a mammalian Ca^{2+} /calmodulin sensitive cyclic nucleotide phosphodiesterase, said method comprising:

10 (a) stably transforming, with a polynucleotide sequence according to claim 1 or 18, a procaryotic or eucaryotic host cell having a phenotypic character susceptible to alteration upon expression of said polynucleotide sequence;

15 (b) growing the host cell formed in step (a) in a nutrient medium under conditions allowing expression of said polynucleotide sequence in said host cell accompanied by the corresponding alteration in the host cell phenotype;

20 (c) identifying said host cells having an altered phenotype;

 (d) disrupting said host cell;

 (e) isolating cytosol from said disrupted host cell;

25 (f) contacting said cytosol with said chemical agent; and

 (g) determining whether said enzymatic activity has been altered.

30 36. An assay method according to claim 35 wherein said host cell is a yeast host cell.

37. An assay method for identifying a chemical agent which modifies the enzymatic activity of a mammalian cyclic GMP stimulated cyclic nucleotide phosphodiesterase, said method comprising:

- 5 (a) stably transforming, with a polynucleotide sequence according to claim 2 or 21, a procaryotic or eucaryotic host cell having a phenotypic character susceptible to alteration upon expression of said polynucleotide sequence in said host;
- 10 (b) growing the host cell formed in step (a) in a nutrient medium under conditions allowing expression of said polynucleotide sequence in said host cell phenotype;
- (c) identifying said host cells having an
15 altered phenotype;
- (d) disrupting said host cell;
- (e) isolating cytosol from said disrupted host cell;
- (f) contacting said cytosol with said chemical
20 agent; and
- (g) determining whether said enzymatic activity has been altered.

38. An assay method according to claim 37 wherein the host cell is a yeast host cell.